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Declaration under Rule 4.17:

— *of inventorship (Rule 4.17(iv)) for US only*

Published:

— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

(88) Date of publication of the international search report:
2 September 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **MINIMALLY IMMUNOGENIC VARIANTS OF HUMANIZED COL-1 ANTIBODY AGAINST CARCINOEMBRYONIC ANTIGEN**

(57) Abstract: The present disclosure provides humanized COL-1 monoclonal antibodies that are minimally immunogenic and that retain carcinoembryonic antigen binding affinity. In one embodiment, a humanized COL-1 antibody includes an amino acid substitution at position 61 in a heavy chain complementarity determining region 2 of the murine COL-1 antibody. In another embodiment, a humanized COL-1 antibody includes an amino acid substitution at position 24, 25, and 27 in a light chain complementarity determining region 1 of the murine COL-1 antibody. In several embodiments, methods are disclosed for the use of a humanized COL-1 antibody in the detection or treatment of a tumor in a subject. Also disclosed is a kit including the humanized COL-1 antibody described herein.

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/27976

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 39/395; C12P 21/04, 21/08; C12N 5/06; C07K 16/00

US CL : 424/133.1, 143.1, 181.1, 183.1; 435/69.6, 328; 530/387.3, 387.7, 388.2, 388.85.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/133.1, 143.1, 181.1, 183.1; 435/69.6, 328; 530/387.3, 387.7, 388.2, 388.85.

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
x --- y	US 6,333,405 B1 (ANDERSON ET AL) 25 Dec. 2001 (25.12.2001), columns 1-2, 4-5, 6 (lines 8-22), 10-13, 15-16.	1-2, 5-6, 11-18. ----- 7, 19, 23-25, 28-35, 37-45, 47-53.
y	KASS E.S. ET AL. Carcinoembryonic antigen as a target for specific antitumor immunotherapy of head and neck cancer. Cancer Research. September 1, 2002, Vol 62, pages 5049-5057, especially pages 5053-5055.	37-45, 47-50.
y	YU B. B. ET AL. Phase I trial of iodine 131-labeled COL-1 in patients with gastrointestinal malignancies: Influence of serum carcinoembryonic antigen and tumor bulk on pharmacokinetics. Journal of Clinical Oncology. June 1996, Vol. 14, No. 6, pages 1798-1809, especially pages 1799 and 1800.	13, 15, 30, 32, 40, 43, 49, 50.
y	RABEN D. ET AL. Enhancement of radiolabeled antibody binding and tumor localization through adenoviral transduction of the human carcinoembryonic antigen gene. Gene Therapy. 1996, Vol. 3, pages 567-580, especially page 567, right column and pages 572, 577-578.	13, 15, 30, 32, 40, 43, 49, 50.



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

14 January 2004 (14.01.2004)

Date of mailing of the international search report

02 JUL 2004

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/27976

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☒ Claim Nos.: 46
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

PCT/US03/27976

Continuation of B. FIELDS SEARCHED Item 3:

WEST, Medline, Biosis, Embase, Cancerlit.

Search terms: COL-1, antibody, humanize, CDR grafting, anti-CEA, PTA-4642, PTA-4643, PTA 4644, immunotherapy, inventor search.